Claims

1. A method for the separation and purification of fibrinogen and at least one other protein which comprises the steps of:

(a) loading a solution comprising fibrinogen and at least one other protein onto an immobilised metal ion affinity chromatography matrix under conditions such that the fibrinogen and the at least one other protein both bind to the matrix, and

(b) selectively eluting the fibrinogen and the at least one other protein separately from the matrix.

2. A method according to claim 1 wherein the at least one other protein is plasminogen.

3. A method for the separation of fibrinogen from plasminogen comprising the steps of:

(a) loading a solution comprising fibrinogen and plasminogen onto an immobilised metal ion affinity chromatography matrix under conditions such that at least the fibrinogen binds to the matrix, and

(b) selectively eluting the fibrinogen from the matrix.

4. A method according to claim 3, wherein the plasminogen and the fibrinogen are selectively eluted separately from the matrix.

5. A method according to any preceding claim wherein the solution comprising fibrinogen is a fibrinogen-containing plasma fraction.

6. A method according to any preceding claim wherein the solution comprising fibrinogen further comprises factor XIII, and the factor XIII is co-eluted with the fibrinogen from the matrix.

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7. A method for the co-purification of fibrinogen and factor XIII which comprises the steps of:

(a) loading a solution comprising fibrinogen and factor XIII onto an immobilised metal ion affinity chromatography matrix under conditions such that the fibrinogen and the factor XIII both bind to the matrix, and

(b) selectively co-eluting the fibrinogen and the factor XIII from the matrix.

8. Use of immobilised metal ion affinity chromatography for the separation of fibrinogen from plasminogen.

9. Use of immobilised metal ion affinity chromatography for the preparation of fibrinogen and plasminogen.

10. Use of immobilised metal ion affinity chromatography for the co-purification of fibrinogen and factor XIII.

11. Fibrinogen prepared by a method according to any of claims 1 to 7.

12. Fibrinogen prepared by a method according to any of claims 1 to 7, for use in therapy.

13. A pharmaceutical kit comprising fibrinogen prepared by a method according to any of claims 1 to 7, together with thrombin.

14. A kit as claimed in claim 13, wherein the thrombin is prepared by a method comprising the steps of:

(a) solvent-detergent virus inactivation of a solution comprising prothrombin and factor X;

(b) loading the product of step (a) onto an anion

exchange medium;

(c) washing the medium to remove the reagents used for the solvent-detergent virus inactivation in step (a);

(d) activating the prothrombin on the medium to form thrombin by the addition of calcium ions; and optionally

(e) selectively eluting the thrombin from the anion exchange medium.

15. A pharmaceutical formulation comprising fibrinogen prepared according to the method of any of claims 1 to 7.

16. A lyophilised fibrinogen formulation comprising fibrinogen prepared according to the method of any of claims 1 to 7, factor XIII, a carbohydrate, an amino acid, a salt, a buffer and a detergent, the formulation being capable of dissolution in water at ambient temperature in less than 15 minutes, preferably less than 10 minutes and more preferably less than 5 minutes to give a fibrinogen solution.

17. A formulation according to claim 16, wherein the concentration of the fibrinogen solution is at least about 60 mg/ml.

18. A formulation according to claim 16 or claim 17, which is heat treated to inactivate viruses.

19. A formulation according to any one of claims 16 to 18, which is free from anti-fibrinolytic agents.

20. A formulation according to any one of claims 16 to 19, which is free from stabilising proteins such as albumin.